

COLONY ARRAY-BASED cDNA LIBRARY NORMALIZATION BY  
HYBRIDIZATIONS OF COMPLEX RNA PROBES AND GENE SPECIFIC  
PROBES

**ABSTRACT**

5        Each cell normally has a widely differing number of mRNA transcribed for each gene. Consequently, a full-length cDNA library constructed from the mRNA would also have a widely differing number of cDNA for each gene. A normalized library of the full-length cDNA of a cell is useful for basic, applied, industrial, and medical research. This invention provides for a method for constructing a normalized  
10      10 full-length cDNA library by probing the members of a non-normalized cDNA library with a library of probes generated from mRNA in order to identify the cDNA of genes that have low or high expression. A collection of the cDNA from the library of the genes that have low expression would constitute a normalized library of these genes. This invention also provides for a method to reduce the number cDNA of genes that  
15      15 have high expression represented by probing these cDNA with a library of probes generated from a small randomly selected number of these cDNA. cDNA that hybridize are represented within this small randomly selected number of cDNA, while cDNA that do not hybridize are not represented. The latter cDNA can undergo further such probing to further reduce the number of cDNA represented. The cDNA from the  
20      20 library of the genes that have low expression and the randomly selected highly expressed cDNA would constitute a normalized library of these genes.